UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

December 20, 2002

OFFICE OF
THE ADMINISTRATOR
EPA SCIENCE ADVISORY BOARD

Note to the Reader:

The attached draft report is a draft report of the EPA Science Advisory Board (SAB). The draft is still undergoing final internal SAB review, however, in its present form, it represents the consensus position of the panel involved in the review. Once approved as final, the report will be transmitted to the EPA Administrator and will become available to the interested public as a final report.

This draft has been released for general information to members of the interested public and to EPA staff. This is consistent with the SAB policy of releasing draft materials only when the Committee involved is comfortable that the document is sufficiently complete to provide useful information to the reader. The reader should remember that this is an unapproved working draft and that the document should not be used to represent official EPA or SAB views or advice. Draft documents at this stage of the process often undergo significant revisions before the final version is approved and published.

The SAB is not soliciting comments on the advice contained herein. However, as a courtesy to the EPA Program Office which is the subject of the SAB review, we have asked them to respond to the issues listed below. Consistent with SAB policy on this matter, the SAB is not obligated to address any responses which it receives. Responses are due no later than INSERT DATE.

1. Has the Committee adequately responded to the questions posed in the Charge?
2. Are any statements or responses made in the draft unclear?
3. Are there any technical errors?

For further information or to respond to the questions above, please contact:

Dr. James Rowe, Designated Federal Officer
EPA Science Advisory Board (1400A)
US Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001
(202) 564-6488 Fax: (202) 501-0582
E-Mail: rowe.james@epa.gov

SAB Executive Committee Review Draft (Jan 14-15, 2003 Meeting)

December 3, 2002

G:\sab\REPORTS\2003report\2003Drafts\LTESWTR DDPB EC Review Draft Dec 03 2002.wpd
EPA-SAB-DWC-03-00X

Honorable Christine Todd Whitman
Administrator
U. S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: Disinfection Byproducts and Surface Water Treatment: A Science Advisory Board Review of Certain Elements of the Stage 2 Regulatory Proposals

Dear Governor Whitman:

This review was conducted by a panel convened in response to a request by the Office of Ground Water and Drinking Water (OGWDW) that the Science Advisory Board (SAB) review several parts of two rules[1] that are being proposed together:

1. The Long Term 2 Enhanced Surface Water Treatment (LT2ESWT) rule.
2. The Stage 2 Disinfectant/Disinfection Byproducts (S2DBP) rule.

The panel consisted of the twelve members of the SAB Drinking Water Committee (DWC) and six consultants.

During September, 2000, a Federal Stakeholder Advisory Committee (Stage 2 Microbial Disinfectants and Disinfection Byproducts Advisory Committee) reached an Agreement in Principle on recommendations for both these “Stage 2" rules after nearly two years of fact finding, deliberation, negotiation, and consensus building. The Stage 1 rules promulgated in 1998, had also been developed after a series of formal negotiations with stakeholders. This report presents the results of the SAB Drinking Water Committee (DWC) review of information provided by EPA on the Stage 2 rules. The LT2ESWT rule is intended to increase protection of public water systems against microbial pathogens, with specific focus on *Cryptosporidium*. The S2DBP rule is intended to increase protection of public water systems from disinfection byproducts, specifically variability in exposure. OGWDW intends to propose and finalize the LT2ESWT and S2DBP rules simultaneously so that systems maintain adequate microbial protection while reducing risk from disinfection byproducts.

[1] Only partial drafts of the two rules were provided; see Sections 3.3, 4.1 for listing of review materials.

The Agency's charges and the Panel's comments follow in abbreviated form:

LT2ESWT Rule:

Charge: The SAB was asked to comment on 1) the analysis of the occurrence (measured, modeled) of a disease-inducing protozoan (*Cryptosporidium)* in drinking water systems, 2) the validity of a risk assessment both before and after applying the proposed treatment methods in the LT2ESWTR to those drinking water distribution systems and 3) the proposed treatment credits (effectiveness in reducing protozoan contamination) by four methods including off-stream water storage, pre-sedimentation, lime softening and reducing water (referred to as microbial toolbox options).

Comments:

1. The Panel commends the Agency on its excellent, groundbreaking work addressing the impact of the proposed regulation on endemic disease (levels of waterborne disease viewed as part of normal community experience). On the other hand, neither the design of the regulation nor the form of the economic analysis directly addresses waterborne outbreaks (events of waterborne disease that stand apart from normal community experience). These outbreaks are the primary stimulus for the regulation and reducing their occurrence could be an important outcome.
2. The modeling of *Cryptosporidium* occurrence appears to be plausible and well done. On the other hand, the economic analysis is necessarily complex and a greater effort is required for effective communication; some statistical issues should be addressed, and estimating the health effects of *Cryptosporidium* should be explored more deeply.
3. The Panel also commends the Agency, as well as the stakeholder process, for developing the bin classification framework[2] as it adds great flexibility to the rule.

The Panel Recommends that EPA:

1. Conduct a systematic review of the design of the LT2ESTW Rule, assessing its effectiveness in addressing outbreaks. Changes should be considered if necessary.
2. Include better graphics in the documentation to help the reader understand the analytical process.
3. Conduct and document sensitivity analyses to the prior distributions and demonstrate the absence of seasonal effects on annual average *Cryptosporidium* concentrations.
4. Provide more information on: a) evidence of endemic disease, b) secondary transmission (e.g., infection from a previously infected person) c) asymptomatic infection (undetected infections with no overt evidence of disease), and d) age effects on host susceptibility to infection and disease.
5. Clarify and justify: a) selection of the dose-response function and whether other models

[2] Determination of regulatory action using a simple classification of water sources based on observed cryptosporidium densities ("bins").

were considered, b) assumptions about oocyst (spore) infectivity, c) assumptions of host susceptibility, and d) estimates of water consumption.

6. Regarding microbial risk assessment: a) compare the approach used to that used by others, b) include a discussion of uncertainties and variability, and c) discuss assumptions which may lead to under- or over-estimation of benefits.
7. For the Bin Classifications: a) for off-stream storage and pre-sedimentation – no credits, b) for two stage lime softening – 0.5 credits, but only if all the water is treated in both stages, and c) for plants that meet special requirements in each filter – 0.5 credits.

S2DBP Rule:

Charge: EPA asked the SAB to comment on: 1) whether the locational running annual average (LRAA) (a new method of estimating concentrations of DBPs) of total trihalomethanes (TTHM)[3] and haloacetic acids (HAA5), in conjunction with the initial distribution system evaluation (IDSE) (recommendations to utilities for identifying appropriate monitoring sites) of the proposed rule more effectively achieves public health protection than the running annual average (RAA) (current method of estimating concentrations of DBPs) of the Stage 1 DBP rule and 2) if the IDSE is capable of identifying new compliance monitoring points that target high TTHM[3] and HAA5 levels and if it is the most appropriate tool available to achieve this objective.

Comments:

1. The Panel believes that some risk reduction will likely occur with the proposed IDSE and LRAA approaches and promulgation of the present rule should not be delayed**.**

2. The proposed Initial Distribution System Evaluation (IDSE) is capable of identifying monitoring points with levels of THM4 and HAA5 that are higher than those currently monitored. However, the IDSE does not consider short-term variations and this should be acknowledged.

3. The locational running annual average (LRAA) will ensure that a larger segment of each community water system will have DBP concentrations below the MCL. While the Panel agrees that these changes are likely to reduce health risk due to DBP exposure, EPA has not demonstrated that this reduction in risk will be in direct proportion to the

[3] These terms refer to by-products of the chlorination process. The Panel believes that the terminology, TTHMs (total trihalomethanes), to represent the four bromine- and chlorine-containing THMs is not adequate since they do not represent the full spectrum of trihalomethanes in drinking water. For example, for some time researchers have also been reporting iodinated THMs in finished drinking water. To avoid confusion regulations that pertain to only the four bromine- and chlorine-containing THMs should refer to these as THM4. A precedent for this form of nomenclature already exists, e.g. HAA5, HAA6, HAA9. For the sake of clarity this report has attempted to employ that nomenclature throughout.

reduction in THM4 and HAA5 concentrations.

Recommendations: The Panel made recommendations that address the charge as well as recommendations that address issues not identified in the charge.

Regarding the charge, the Panel recommends that EPA:

1. Pursue the concept of locational running annual averages (LRAAs) as a more effective means of controlling exposure to harmful compounds in the drinking water than system-wide running annual averages (RAAs).
2. Identify temporal limitations in the IDSE documentation and require periodic reevaluation of selected sites.
3. Reallocate the samples so that, for both free chlorine and chloramines, sampling takes into account potential high THM4 and HAA5 sites.
4. Require the measurement and reporting of residual chlorine and individual THM4 and HAA5 species.
5. Provide more guidance to utilities to identify sampling sites with highest HAA5 concentrations.
6. Improve the proposed system specific studies (SSS) approach.
7. Reconsider the use of the SWAT(Surface Water Analytical Tool) model and ICR (Information Collection Rule) data in economic analyses or risk reduction calculations.

Beyond the charge: It is critical to address the limitations inherent in the use of the surrogates (THM4, HAA5) to represent the full spectrum of DBPs present in drinking water. **Therefore the Panel further recommends that EPA:**

1. Focus its future research program upon identifying causal agents for bladder cancer and other adverse health effects associated with chlorinated drinking water in epidemiological studies.
2. Link future control strategies for DBPs more directly to the reduction of these causal agents.

Thank you for the opportunity to review these proposals. We would be happy to continue to engage with EPA as it pursues this action. We look forward to your response to this report.

Sincerely,

Dr. William Glaze, Chair
EPA Science Advisory Board

Dr. R. Rhodes Trussell, Chair
Drinking Water Committee
EPA Science Advisory Board

NOTICE

This report has been written as part of the activities of the Science Advisory Board, a public advisory group providing extramural scientific information and advice to the Administrator and other officials of the Environmental Protection Agency. The Board is structured to provide balanced, expert assessment of scientific matters related to problems facing the Agency. This report has not been reviewed for approval by the Agency and, hence, the contents of this report do not necessarily represent the views and policies of the Environmental Protection Agency, nor of other agencies in the Executive Branch of the Federal government, nor does mention of trade names or commercial products constitute a recommendation for use.

Distribution and Availability: This EPA Science Advisory Board report is provided to the EPA Administrator, senior Agency management, appropriate program staff, interested members of the public, and is posted on the SAB website (www.epa.gov/sab). Information on its availability is also provided in the SAB monthly newsletter (Happenings at the Science Advisory Board). Additional copies and further information are available from the SAB Staff [US EPA Science Advisory Board (1400A0, 1200 Pennsylvania Avenue, NW, Washington, DC 20460-0001; (202) 564-4533)].

U.S. Environmental Protection Agency
Science Advisory Board
Drinking Water Committee
Stage 2 DBP/Surface Water Treatment Rule Review Panel

CHAIR

Dr. R. Rhodes Trussell, MWH, Inc. Pasadena, CA.

MEMBERS

Dr. David B. Baker, Heidelberg College, Water Quality Laboratory, Tiffin, OH

Dr. Mary Davis, West Virginia University, Health Sciences Center, Morgantown, WV

Dr. Ricardo De Leon, Metropolitan Water District of Southern California, Water Quality Laboratory, La Verne, CA

Dr. Sidney Green, Howard University, Department of Medicine, Washington, DC

Dr. Barbara Harper, Yakima Indian Nation, Richland, WA

Dr. Lee D. (L.D.) McMullen, Des Moines Water Works, Des Moines, IA

Dr. Christine Moe, Emory University, Rollins School of Public Health, Atlanta, GA

Dr. Philip Singer, University of North Carolina, School of Public Health, Chapel Hill, NC

Dr. Gary A. Toranzos, University of Puerto Rico, San Juan, PR

OTHER SAB MEMBERS

Dr. Richard Bull, MoBull Consulting, Inc., Kennewick, WA

Dr. Lauren Zeise, California Environmental Protection Agency, Office of Environmental Health Hazard Assessment, Oakland, CA

CONSULTANTS

Dr. Mark Benjamin, University of Washington, Seattle, WA

Dr. L. Mark Berliner, Ohio State University, Department of Statistics, Columbus, OH

Dr. Paul Boulos, MWH Soft, Inc., Broomfield, CO

Dr. Michael J. Daniels, University of Florida, Department of Statistics, Gainesville, FL

Dr. Gregory Harrington, University of Wisconsin, Department of Civil and Environmental Engineering, Madison, WI

Dr. Charles O'Melia, The Johns Hopkins University, Department of Geography and Environmental Engineering, Baltimore, MD

LISAISONS

Dr. David P. Spath, California Department of Health Services, Division of Drinking Water and Environmental Management, Sacramento, CA

SCIENCE ADVISORY BOARD STAFF

Mr. Thomas O. Miller, Designated Federal Official, US EPA Science Advisory Board (1400A), 1200 Pennsylvania Avenue, NW, Washington, DC

Dr. James N. Rowe, Designated Federal Official, US EPA Science Advisory Board (1400A), 1200 Pennsylvania Avenue, NW, Washington, DC

Ms. Wanda Fields, Management Assistant, US EPA Science Advisory Board (1400A), 1200 Pennsylvania Avenue, NW, Washington, DC

TABLE OF CONTENTS

1. EXECUTIVE SUMMARY

The Drinking Water Committee (DWC) of EPA's Science Advisory Board (SAB) met to consider several support documents that are a part of the EPA Long Term 2 Enhanced Surface Water Treatment (LT2ESWT) rule and the Stage 2 Disinfectant/Disinfection Byproducts (S2DBP) rule, both of which are under development by the Agency. During September, 2000, a Federal Stakeholder Advisory Committee reached an Agreement in Principle on recommendations for both these Stage 2 rules after nearly two years of fact finding, deliberation, negotiation, and consensus building. The Stage 1 rule promulgated in 1998, had also been developed after a series of formal negotiations with stakeholders. This report presents the results of the SAB Drinking Water Committee (DWC) review of information provided by EPA on the Stage 2 rules.

The 1996 Amendments to the Safe Drinking Water Act (SDWA) require EPA to develop National Primary Drinking Water Regulations (NPDWRs) for contaminants which have an adverse effect on the health of persons and where regulation provides a meaningful opportunity for public health protection. EPA is developing a LT2ESWT rule to provide increased protection for public water systems against microbial pathogens, with a specific focus on *Cryptosporidium*. The proposed rule is intended to supplement existing surface water treatment rules by establishing targeted treatment requirements for systems with greater vulnerability to *Cryptosporidium*. Such systems include those with high concentrations of *Cryptosporidium* in their source water and those that do not provide filtration. In addition, the 1996 SDWA Amendments require EPA to develop a S2DBP rule. The intent of the proposed S2DBP rule is to reduce the variability of exposure to disinfection byproducts for people served at different points in the distribution systems of public water supplies. EPA has suggested that this decreased exposure will result in reduced risks from potential reproductive and developmental health effects and cancer. To be consistent with the SDWA requirements for risk balancing, EPA intends to propose and finalize the LT2ESWT and the S2DBP rules simultaneously. This coordinated approach is designed to ensure that systems maintain adequate microbial protection while reducing risk from disinfection byproducts.

The Panel believes that the terminology, TTHMs (total trihalomethanes), to represent the four bromine- and chlorine-containing THMs is not adequate since they do not represent the full spectrum of trihalomethanes present in drinking water. For example, for some time researchers have also been reporting iodinated THMs in finished drinking water. To avoid confusion regulations that pertain to only the four bromine- and chlorine-containing THMs should refer to these as THM4. A precedent for this form of nomenclature already exists, e.g. HAA5, HAA6, HAA9. For the sake of clarity this report has attempted to employ that nomenclature throughout.

This report has two major parts reflecting the structure of the Agency Charge. The charge to the SAB Panel for the Long Term-2 Enhanced Surface Water Treatment rule asked the SAB to comment on: 1) the analysis of *Cryptosporidium* occurrence; 2) the pre- and post-LT2ESWTR *Cryptosporidium* risk assessment; and 3) the proposed treatment credits for four microbial toolbox options. For the Stage 2 DBP rule, EPA asked the SAB to comment on: 1) whether the

locational running annual average (LRAA) for total trihalomethanes (TTHM) and haloacetic acids (HAA5), in conjunction with the initial distribution system evaluation (IDSE), of the proposed rule more effectively achieve public health protection than the running annual average (RAA) of the Stage 1 DBP rule and 2) if the IDSE is capable of identifying new compliance monitoring points that target high TTHM and HAA5 levels and if it is the most appropriate tool available to achieve this objective.

For the **LT2ESWTR**, because the risk assessment is quite complex, the Panel recommends that the document include graphics that show how the different elements were derived and how they relate to each other. For clarity, comments and recommendations are presented separately for the three charge questions related to the risk assessment.

First, the Panel concludes that the occurrence modeling appears to be both plausible and well-done. However, the Panel believes that a number of issues need to be addressed, either by supplementing the current documents and/or modifying the model.

The Panel recommends that the Agency:

1) Conduct and document sensitivity analyses to the prior distributions and,
2) Demonstrate the absence of seasonal effects on the annual average *Cryptosporidium* concentration.

Secondly, for the microbiological risk assessment review, each of the basic elements was examined in order: hazard identification, dose-response assessment, and exposure assessment. Then the outcome of the risk assessment was evaluated. Two criteria were considered in the Panel evaluation: a) whether the Agency assumptions were transparent, and b) whether scientific evidence exists to support the assumptions. *Cryptosporidium parvum* has been responsible for significant waterborne disease outbreaks, and it is likely that the organism is responsible for significant endemic disease as well. Both of these outcomes are important. The current form of the Agency's analysis (The Cadmus Group, Inc., 2001b) for the LT2ESWTR does an excellent job of addressing the impact of drinking water quality on the incidence of endemic disease and the health risk reduction that will result from the reduction of endemic disease as a result of the proposed regulation. The Agency is to be congratulated for this ground-breaking work. On the other hand, in the present draft, neither the design of the regulation nor the contents of the Agency analysis directly address waterborne outbreaks. These outbreaks are the primary stimulus for the regulation and reducing their occurrence should be one of the most important potential outcomes from the regulation as well. The Panel recommends that EPA conduct a systematic review of the design of the LT2ESWTR regulation keeping its effectiveness in addressing waterborne outbreaks in mind.

- The Panel agree with the basic information on *Cryptosporidium* health effects in the Hazard Identification section but recommends that the following be included in the analysis: 1) evidence of current prevalence of endemic disease, 2) information on secondary transmission of cryptosporidiosis, and 3) host age and frequency of asymptomatic infections.

- For the Dose-Response Assessment, the Panel recommends clarification and justification of: 1) the basis for the selection of the dose response function that was used and whether other models were considered, 2) the term "infectivity" as it is used in the EPA analyses, 3) the assumptions about infectivity of oocysts used in human dosing experiments, infectivity of oocysts found in environmental samples and of the significance of *Cryptosporidium* genotype when evaluating infectivity for humans, and, 3) assumptions about variability in host susceptibility, both due to possible immunity resulting from previous infections and due to other susceptibility factors such as age and health.

- For Exposure Assessment, the estimates of consumption require clarification.

- For the Risk Assessment, the Panel notes that quantitative microbial risk assessment is a rapidly developing field. The Agency should 1) identify other approaches to microbial risk assessment, especially risk assessments for Cryptosporidium, that are reported in the literature and consider how they compare to their own assessment, 2) include a discussion of uncertainties and variability, and 3) discuss assumptions which may lead to underestimates or overestimates of risk and benefits.

Finally, for the treatment credits for the four microbial toolbox options, the Panel commends the EPA, as well as the stakeholder process used, for developing the bin classification framework for identifying the treatment requirements for drinking water and the microbial toolbox containing possible treatment options to guide systems having treatment needs. These alternatives add great flexibility for meeting varying water quality and treatment options and should result in safe drinking water for the people of the United States. The Agency charged the Panel with evaluating EPA information on four of the toolbox options: 1) off stream raw water storage; 2) pre-sedimentation, 3) lime softening and 4) lower finished water turbidity. Specifically, the Agency asked the Panel to comment on the credits that have been proposed for specific toolbox options for *Cryptosporidium* removal. In summary, the Panel recommends that no presumptive credits be given for off-stream storage and pre-sedimentation. It does agree with giving 0.5 log credit for two-stage lime softening if all the water is treated with both stages, and 0.5 log credit for plants that demonstrate a turbidity level in each individual filter effluent less than or equal to 0.15 NTU in at least 95 percent of the measurements taken each month. Details about these recommendations are found in the report.

For the **Stage 2 DBP rule**, the Panel believes that the proposed Initial Distribution System Evaluation is capable of identifying new compliance monitoring points that target higher THM and HAA levels than are currently measured in the existing THM Rule and Stage 1 DBP Rule compliance monitoring programs. However, the IDSE does not consider short-term, temporal variations that occur at different sites in the distribution system due to varying water demands and distribution system architecture and operation. This temporal variability needs to be acknowledged in the IDSE documentation. The Panel further believes that the proposed standard monitoring program (SMP) for sub-part H systems serving more than 10, 000 people is reasonable; however, the Panel does make some recommendations concerning the proposed sampling requirements. The switch from the running annual average (RAA) approach to the

locational running annual average (LRAA) approach provides a measure of equity not previously reflected in the standards for disinfection by-products. The LRAA allows one to state that a larger segment of the consumers will be provided with drinking water within a particular water system which will meet the MCL than the RAA approach. The Panel also agrees that these changes are likely to result in a reduction in health risk due to DBP exposure, but EPA has not demonstrated that this reduction in health risk will be in direct proportion to the reduction in the THM and HAA5 concentrations.

The Committee recommends that in proposing its Stage 2 DBP rule, the Agency:

- Pursue the concept of locational running annual averages (LRAAs) as a more effective means of controlling exposure to harmful compounds in the drinking water than system-wide running annual averages (RAAs).
- Identify temporal limitations in the IDSE documentation and require periodic reevaluation of selected sites;
- Reallocate the samples so that, for both free chlorine and chloramines, sampling takes into account potential high THM and HAA sites;
- Require the measurement and reporting of residual chlorine and individual THM and HAA species;
- Provide more guidance to utilities to identify sampling sites with highest HAA concentrations;
- Improve the proposed system specific studies (SSS) approach (Chapter 6);
- Reconsider the use of the SWAT model and ICR data in economic analyses or risk reduction calculations;
- Focus their research program upon identifying causal agents for bladder cancer and other potential adverse health effects associated with chlorinated drinking water; and,
- Link control strategies for DBPs to reduction of causal factors of health effects.

2. INTRODUCTION AND CHARGE

2.1 Introduction

The 1996 Amendments to the Safe Drinking Water Act (SDWA) require EPA to develop National Primary Drinking Water Regulations (NPDWRs) for contaminants which have an adverse effect on the health of persons and where regulation provides a meaningful opportunity for public health protection. EPA is developing a Long Term 2 Enhanced Surface Water Treatment (LT2ESWT) rule to provide increased protection for public water systems against microbial pathogens, with a specific focus on *Cryptosporidium*. The proposed rule is intended to supplement existing surface water treatment rules by establishing targeted treatment requirements for systems with greater vulnerability to *Cryptosporidium*. Such systems include those with high concentrations of *Cryptosporidium* in their source water and those that do not provide filtration.

In addition, the 1996 SDWA Amendments require EPA to develop a Stage 2 Disinfectant/Disinfection Byproducts (S2DBP) rule. The intent of the proposed S2DBP rule is to reduce the variability of exposure to disinfection byproducts for people served at different points in the distribution systems of public water supplies. EPA has suggested that this decreased exposure will result in reduced risks from potential reproductive and developmental health effects and cancer.

To be consistent with the SDWA requirements for risk balancing, EPA intends to propose and finalize the LT2ESWT and the S2DBP rules simultaneously. This coordinated approach is designed to ensure that systems maintain adequate microbial protection while reducing risk from disinfection byproducts. During September, 2000, a Federal Stakeholder Advisory Committee reached an Agreement in Principle on recommendations for both these rules after nearly two years of fact finding, deliberation, negotiation, and consensus building. Prior to that, the Stage 1 rules for DBPs and surface water treatment also reflected periods of formal regulatory negotiations and stakeholder discussions over a period of years stretching from the early to mid-1990s.

The Panel believes that the terminology, TTHMs (total trihalomethanes), to represent the four bromine- and chlorine-containing THMs is not adequate since they do not represent the full spectrum of trihalomethanes in drinking water. For example, for some time researchers have also been reporting iodinated THMs in finished drinking water. To avoid confusion regulations that pertain to only the four bromine- and chlorine-containing THMs should refer to these as THM4. A precedent for this form of nomenclature already exists, e.g. HAA5, HAA6, HAA9. For the sake of clarity this report has attempted to employ that nomenclature throughout

The EPA Office of Ground Water and Drinking Water (OGWDW) representatives requested that the Science Advisory Board (SAB) review several parts of the LT2ESWT and the S2DBP rule proposals and certain support documents and provide advice in response to a

number of charge questions. This report presents the results of the SAB Drinking Water Committee (DWC) review of these issues.

2.2 The Charge

The Agency charge to the SAB Panel for the Long Term-2 Enhanced Surface Water Treatment rule asked the SAB to comment on: 1) the analysis of *Cryptosporidium* occurrence; 2) the pre- and post-LT2ESWTR *Cryptosporidium* risk assessment; and 3) the proposed treatment credits for four microbial toolbox options.

For the Stage 2 DBP rule, EPA asked the SAB to comment on: 1) whether the locational running annual average (LRAA) for total trihalomethanes (TTHM) and haloacetic acids (HAA5), in conjunction with the initial distribution system evaluation (IDSE), of the proposed rule more effectively achieves public health protection than the running annual average (RAA) of the Stage 1 DBP rule and 2) if the IDSE is capable of identifying new compliance monitoring points that target high TTHM and HAA5 levels and if it is the most appropriate tool available to achieve this objective.

3. LONG TERM 2 ENHANCED SURFACE WATER TREATMENT RULE

3.1 Introduction

EPA convened a group of stakeholders, including EPA itself, to hold formal negotiations on issues related to the LT2ESWT and Stage 2 DBP rules from 1999 to 2000. Their Agreement in Principle, which contains recommendations for the proposed LT2ESWT and Stage 2 DBP rules, was published in the Federal Register on December 29, 2000 (EPA, 2000).

In general, because the risk assessment is quite complex, the Panel recommends that the document include more graphics to illustrate how the different elements of the model were derived and how they relate to each other. Exhibit 5.2 (The Cadmus Group, Inc., 2001b) is helpful but does not provide sufficient detail. Additional figures are needed to show what elements were in the pre-regulation risk assessment versus the post-regulation risk assessment and how the reduction in risk from the proposed regulation was calculated. Figures 3.1 through 3.4 of this report are examples displaying the Panel's understanding based on its reading of the documents provided by EPA and its discussions with EPA personnel.

3.2 Charge Question 1: Analysis of Cryptosporidium occurrence

EPA requested SAB comments on the Agency analysis of Cryptosporidium occurrence.

EPA provided the Panel with a draft document entitled *Occurrence and Exposure Assessment for the Long Term 2 Enhanced Surface Water Treatment Rule*. (The Cadmus Group, 2001a) that discusses how EPA estimated the occurrence distribution of *Cryptosporidium* in the source and finished water of public water systems prior to implementation of a new LT2ESWT rule. Sections of the document considered to be of particular importance discussed the data sources used to estimate *Cryptosporidium* occurrence in source water, along with analytical methods, data quality issues, and the statistical techniques used to model occurrence distributions; information on observed and modeled results from the source water occurrence surveys; information from studies of the physical removal of *Cryptosporidium* by treatment processes; finished water occurrence data resulting from the Information Collection Rule (ICR); a description of how EPA estimated finished water *Cryptosporidium* levels prior to implementation of the LT2ESWTR; and technical information on the statistical models used to analyze source water occurrence data.

3.2.1 Panel Response to LT2ESWTR Charge Question 1--Analysis of Cryptosporidium occurrence

3.2.1.1 Background

The model developed by EPA can be thought of in three parts (Figure 3-1). The first part is designed to address an important limitation of the data collected in the ICR and ICR Supplemental Survey (ICRSS), namely information on the national occurrence of *Cryptosporidium parvum* oocysts at levels below the detection limits (DLs) of the methods used in those surveys. Thus, the first part simulates national distributions of the concentration of *C. parvum* oocysts in the source water. Using ICR and ICRSS data, the model is designed to produce an estimate of the national occurrence of oocysts in untreated surface waters, above and below the ICR and ICRSS DLs. Bayesian hierarchical models and Markov chain Monte Carlo methods are used to accomplish this (Figure 3-2). These models accommodate the many complex features seen in the data used by EPA to develop its national occurrence estimates, including low recovery probabilities, the presence of false positives, and the presence of true *Cryptosporidium*-free source waters.

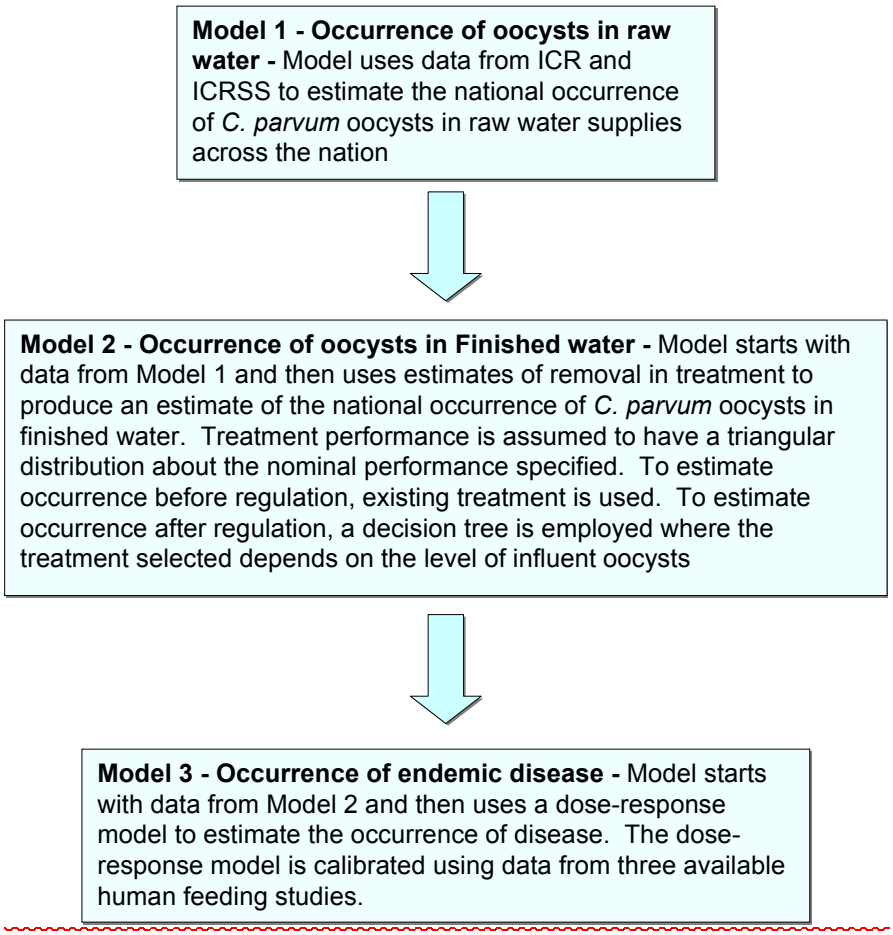

Figure 3-1. The model developed by the EPA contains three components. The first uses data from the ICR and ICRSS to produce a national distribution of *C. parvum* oocysts in untreated surface water. The second uses that national distribution and a model of treatment performance to produce a simulation of the national distribution of *C. parvum* oocysts in finished water. The third component uses a dose-response model calibrated via human exposure studies, data on water consumption, and finished water oocyst levels to predict the level of endemic disease.

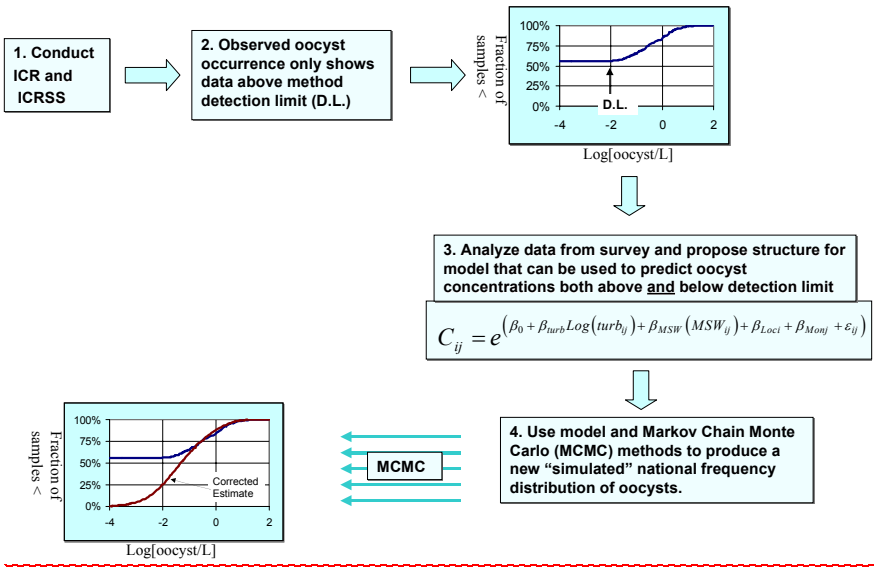

Figure 3-2. Model 1: Occurrence of oocysts in raw water - Bayesian hierarchial models and Markov Chain Monte Carlo Methods were used to estimate the national occurrence of *C. parvum* oocysts in raw water

The second part of the model takes the national occurrence in untreated water from the first part and uses treatment assumptions to produce an estimate of the national occurrence of *C. parvum* oocysts in treated water (Figure 3-3). To estimate occurrence before regulation, treatment credits in the existing Interim Enhanced Surface Water Treatment Rule (IEWSTR) are used. The proposed regulation assigns water systems into various bins depending on the level of oocysts in their untreated water. A higher degree of removal is required for systems with untreated water falling into bins that correspond to higher oocyst concentrations. To estimate occurrence after regulation, treatment is assumed to meet the requirements that correspond to the bin selected for each supply. For the analysis in this second part, EPA assumed that treatment effectiveness is independent of concentration and, based on expert opinion, treatment effectiveness across the nation is assumed to follow a simple triangular distribution with the mode at the performance specified by the rule.

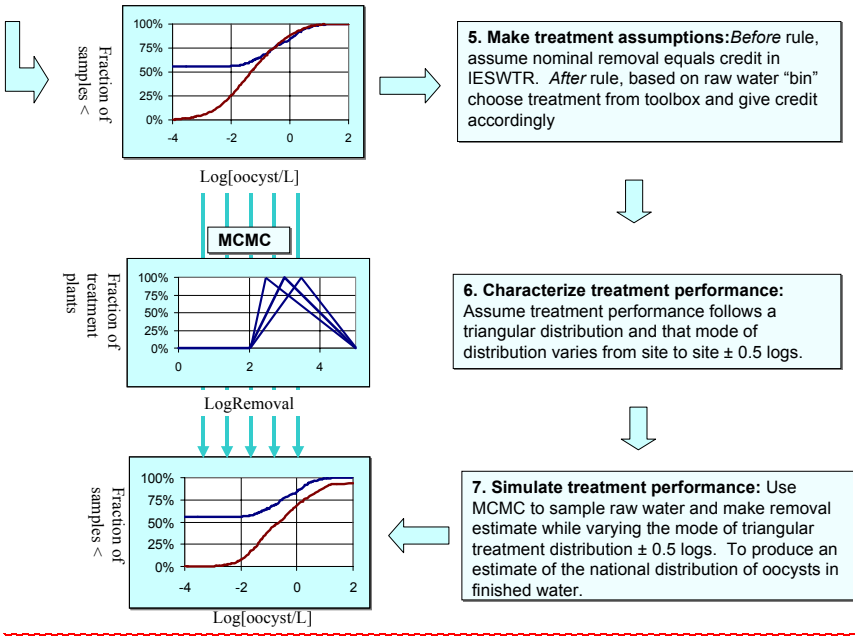

Figure 3-3. Model 2 - Occurrence of oocysts in Finished water - Treatment performance is assumed to have a triangular distribution. Before regulation, existing treatment is assumed to meet the IESWTR. After regulation, a decision tree is employed where the treatment selected depends on the level of influent oocysts (the bin).

The third part of the model estimates the national occurrence of disease. The model uses the national occurrence of *C. parvum* oocysts in finished water and combines it with data on water consumption and on dose-response to produce an estimate of disease. The model considers the distribution of infection (and disease) conditional on the concentration of viable oocysts in the drinking water through the use of an exponential dose-response model. The parameters of the dose-response model were estimated using data from three human dosing studies. A Bayesian hierarchical model is also used here to model the distribution of infectivity across *Cryptosporidium* strains. To predict the occurrence of disease, Monte Carlo methods are used to sample oocyst concentrations in finished water and volumes of water consumed and estimate disease using the dose-response model (Figure 3-4).

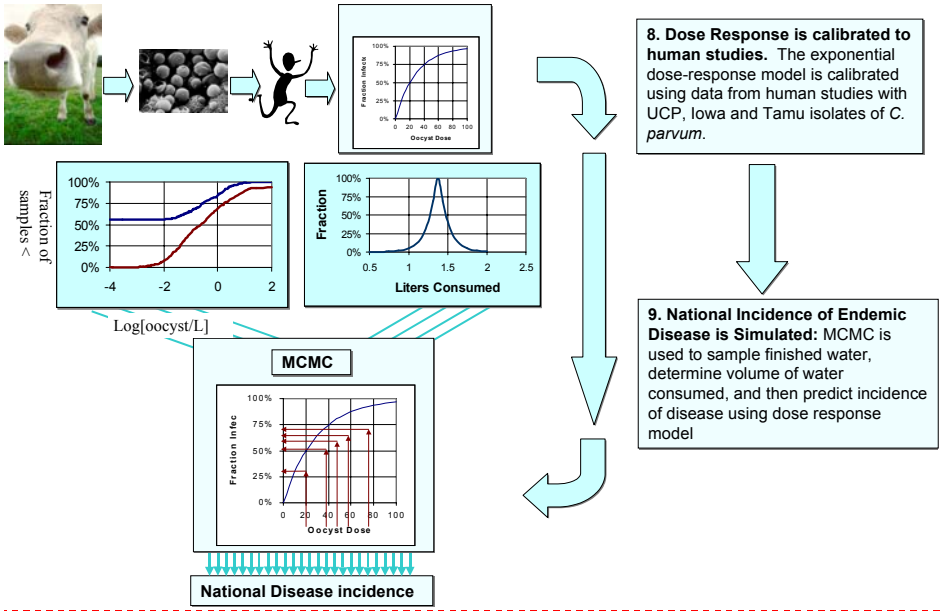

Figure 3-4. Model 3 - Occurrence of endemic disease - Human feeding studies are used to calibrate the dose-response model and then MCMC methods are used to sample from finished water, determine the liters consumed and estimate the national incidence of endemic disease

Monte Carlo integration is used throughout the model and, for the first and third parts of the model, Markov chain Monte Carlo (MCMC) methods were used to sample from posterior distributions which are used to both estimate parameters in the model and to address the uncertainty associated with these parameters. In complex Bayesian models, MCMC is the appropriate way to do this. Both parts two and three of the model must be re-run each time different regulations or different treatment conditions must be considered.

Immediately below, is a discussion of some specific issues regarding the first piece of the model, the national occurrence distribution of *Cryptosporidium*.

3.2.1.2 Panel Conclusions

First, the Panel concludes that the occurrence modeling appears to be both plausible and well-done. However, the Panel believes that a number of issues need to be addressed, either by supplementing the current documents and/or modifying the model.

The Panel recommends that sensitivity analyses of the modeling effort be conducted and documented. A key component in Bayesian hierarchical models is the specification of prior distributions, which *a priori*, characterize the state of knowledge about the parameters at the higher levels of the model. Little information is contained about such priors in the current documentation and it is not evident that the sensitivity of the occurrence distribution and the

infectivity parameter, k, to these priors has been assessed. Sensitivity analyses should be conducted and documented. Particular concerns arise when the data are used to assess the model and direct the selection of prior distributions. While such practices are sometimes needed in difficult problems, they can result in underestimation of uncertainty due to the double use of the data. The analysts need to be clear about whether or not such methods were used, and if so, how the final uncertainties may be impacted. Much of the concern can be ameliorated through complete sensitivity analysis.

The Panel also recommends that seasonal effects be more carefully addressed. In the Panel's opinion, the absence of seasonal effects on the annual average *Cryptosporidium* concentration has not been demonstrated. The Agency should address and clarify its computation of the average *Cryptosporidium* concentration for plants in a system over the 18-month period for which the data were collected in the Information Collection Rule (ICR). Averaging concentrations equally over the 18 months to obtain an annual average will only give an unbiased estimate of the true annual average if there are no seasonal effects. But the absence of seasonal effects has not been demonstrated. The current approach effectively counts six months twice in the averaging. During discussions at the DWC meeting in December 2001, EPA representatives stated that parameters characterizing seasonality were included in the model (in the form of the turbidity term). This problem, might be addressed by averaging the data by month, and then to using the mean of the resulting twelve monthly averages as the annual average.

The Panel believes that a number of other improvements would also strengthen the Agency's LT2ESWTR documentation. Additional model checking should be conducted. The current EPA report includes some model-checking using the estimated distributions of true concentrations, but the Panel recommends additional model checking, specifically, an additional internal check and an external check. The internal check could use the current output from the MCMC sampler to sample from the distribution of predicted oocyst counts (Y) (from the posterior predictive distribution of Y) . To assess how consistent predictions from the model are with the observed data, about twenty sample distributions can be plotted versus the observed distribution of counts. The observed distribution ideally should lie within these 20 and should look similar. For an external check, the current model could be fit to the first 12 months of the 18 month ICR data, then months 13-18 could be predicted by the model and finally these predictions could be compared to the observed data.

There are some additional features that could be included in the documentation to improve the clarity of the Agency's analyses. A map of the sites for both the ICR and Information Rule Supplemental Survey (ICRSS) data would be helpful to see how similar the spatial distribution of sites was across the surveys and to also look for spatial similarity in concentrations for sites close together and/or in the same regions of the country. In addition, the Panel recommends that a short paragraph be added documenting the convergence and mixing checks on the MCMC sampler. An additional issue of moderate importance is that several parameters that were included in the filtered model are excluded in the discussion of the model for the unfiltered plants (e.g., turbidity). Justification for this would improve the clarity of EPA's analysis.

The Panel notes that the Agency approach to concisely summarize the occurrence distribution functions using parametric models, in particular the log normal function, was done to simplify computations for the individuals conducting the risk analysis. Documentation could be made available to confirm that the realizations of the cumulative distribution functions (CDFs) from the MCMC sampler were well approximated by log-normal cumulative distribution functions (CDFs). Second, several *ad hoc* simplifications were done to sample the CDF for the risk analysis (see bottom of p. 5-15 of the economic analysis document, The Cadmus Group, Inc. 2001b). The Panel recommends that these be examined carefully for their plausibility and the conclusions documented.

The Panel concluded that there is a large amount of uncertainty in the modeling of the occurrence of *Cryptosporidium*. For example, the occurrence distributions are estimated based on only one year of data. This will be fine if these distributions are stable over years. However, the current data does not allow determination if the particular year in which the data were collected were aberrant (for example, due to weather patterns) or if there is some sort of trend in occurrence over time. In addition, for the infectivity modeling, the distribution of infectivity across strains is estimated based on only three *Cryptosporidium* strains which may or may not be a random sample of strains. The only way this distribution can be estimated is to make a strong assumption about its form (here it is assumed to be log-normal). The ultimate accuracy of the predicted decrease in disease from these stochastic models relies on both the representativeness and applicability of the observed data and the numerous modeling assumptions that were made in the course of the three pieces of the model discussed at the beginning of this section. This qualification should be noted in the document.

3.3 Charge Question 2: Pre- and post-LT2ESWTR Cryptosporidium risk assessment

EPA requested SAB comments on the pre- and post-LT2ESWTR Cryptosporidium risk assessment.

EPA provided the Panel with partial drafts of documents entitled: 1) *Economic Analysis for the Long Term 2 Enhanced Surface Water Treatment Rule* (The Cadmus Group, Inc., 2001b) and *2) Appendices to the Economic Analysis for the Long Term 2 Enhanced Surface Water Treatment Rule* (The Cadmus Group, Inc., 2001c). These documents show how EPA estimated the incidence of endemic cryptosporidiosis attributable to drinking water both prior to and following implementation of the LT2ESWTR. Information in the documents considered by EPA to be of particular relevance included:

a) a summary of the LT2ESWTR to be proposed, based on the Stage 2 M-DBP Advisory Committee Agreement in Principle;
b) baseline information used to conduct the risk assessment;
c) descriptions of how EPA modeled pre- and post-LT2ESWTR risk of cryptosporidiosis;
d) a summary of how EPA predicted the technologies that filtered and unfiltered systems would select to comply with the LT2ESWTR;

e) descriptions of how EPA estimated the percentage of plants expected to receive 0.5 and 1.0 log additional *Cryptosporidium* treatment credit under the LT2ESWTR;
f) details on estimates of the percent of systems that would be assigned to different bins as a result of source water monitoring under the LT2ESWTR;
g) distributions of risk of illness;
h) unit costs for treatment technologies;
i) descriptions of the methodology used to forecast the percentage of plants assigned to a given bin that would select a particular technology;
j) results of the technology selection forecast;
k) total treatment costs for different system categories associated with different regulatory alternatives and assumptions about technology availability;

3.3.1 Panel Response to LT2ESWTR Charge Question 2

This SAB review panel included experts in statistical modeling, in public health microbiology and engineering, but it did not include specialists in quantitative microbiological risk analysis, a relatively new field. For the review, each of the basic elements of microbial risk assessment was examined in order: hazard identification, dose-response assessment, and exposure assessment. Then the outcome of the risk assessment was evaluated. Two criteria were considered in the Panel evaluation: a) whether the Agency assumptions were transparent, and b) whether scientific evidence exists to support the assumptions.

Cryptosporidium parvum has been responsible for significant waterborne disease outbreaks, and it is likely that the organism is responsible for significant endemic disease as well. Both of these outcomes are important. The current form of the Agency's analysis (The Cadmus Group, Inc., 2001b) for the LT2ESWTR does an excellent job of addressing the impact of drinking water quality on the incidence of endemic disease and the health risk reduction that will result from the reduction of endemic disease as a result of the proposed regulation. The Agency is to be congratulated for this ground-breaking work.

On the other hand, in the present draft, neither the design of the regulation nor the contents of the Agency analysis directly address waterborne outbreaks. These outbreaks are the primary stimulus for the regulation and reducing their occurrence should be one of the most important potential outcomes from the regulation as well.

The Panel recommends that EPA conduct a systematic review of the design of the LT2ESWTR regulation and evaluate its effectiveness in addressing waterborne outbreaks. This review should include an examination of the causes of past outbreaks and how the proposed regulatory framework will address those causes. The Agency should then consider if any changes in the framework must be made. Additional consultation with specialists in quantitative microbial risk assessment could be of benefit to the Agency as it completes its consideration of *Cryptosporidium* risks.

3.3.1.1 Hazard Identification

The Panel agreed with the basic information on Cryptosporidium health effects that were presented in this section. See pages 5-7 - 5-8 of the *Economic Analysis for the Long Term 2 Enhanced Surface Water Treatment Rule* (US EPA 2001b). There are a few additional areas that should also be included in the analysis:

a) **Evidence of current prevalence of endemic disease**. EPA's analysis is based on reduction of endemic disease. Some direct evidence of endemic disease levels would greatly strengthen the case. Perhaps the results of serological studies could be used to indicate about the prevalence of *Cryptosporidium* exposure/infection in the US.

b) **Information on secondary transmission of cryptosporidiosis**. The current analysis does not consider secondary transmission of the disease. This decision should have stronger support in the documentation or should be reconsidered. Haas et al. (1999) present data on prevalence of secondary cases of cryptosporidiosis from two outbreak investigations that range from 4 - 33%. Other data in the published research literature, and perhaps data from the Centers for Disease Control may provide the basis for estimating the magnitude of secondary transmission [e.g., household via child (e.g., Newman et al., 1994), household via adult (MacKenzie et al., 1995), child care centers, swimming pools (Puech et al., 2001; Sorvillo et al., 2001); Millard, et al., 1994]. Asymptomatic infections may play an important role in secondary transmission of infection. Failure to consider secondary transmission will likely underestimate the impact of the LT2ESWTR on reducing the risks of cryptosporidiosis.

c) **Age Effects**. Information on the prevalence of asymptomatic *Cryptosporidium* infections by age should be included in the hazard identification.

3.2.1.2 Dose-Response Assessment

For the dose-response component of the risk assessment, the Panel comments on four areas of the assessment: a) selection of a dose-response function, b) use of the term infectivity, c) the morbidity rate, and d) the mortality rate.

a) Clarify the Basis for Selection of a Dose Response Function

The general exponential model was used to characterize the dose-response relationship based on the data from three human challenge studies. Modeling this relationship is important for estimating the risk of infection at low doses because it is not economical to conduct large human challenge studies to directly measure infection rates. The choice of the exponential dose-response model is reasonable and has been used in previous cryptosporidiosis risk assessments (Haas et al., 1996, 1999). But it is not clear if other models were considered and fit to the data from the human challenge studies. The Panel recommends that EPA document the models that were considered and the reasons for selecting this particular one.

b) Clarify the Use of the Term Infectivity in EPA Analysis

A number of aspects of infectivity that are described in EPA's analysis (pages 5-10) deserve further discussion. Among these things are: i) the use of the proportion of the total oocysts from the occurrence estimates that have internal structures to determine the fraction of oocysts considered infectious, ii) the fraction of the oocysts from the three strains of *C. parvum* used in the human challenge studies (IOWA, TAMU and UCP) which were considered infectious and iii) the relationship between the two, namely the fraction of oocysts that were infectious in the human studies versus the fraction of the oocysts that were infectious in environmental samples (i.e., the parameter "v" in the equation below).

Infectivity of oocysts in the environment: The assumptions about the proportion of infectious oocysts in the environment determine the variable v used in the EPA equation for estimating morbidity:

$$P_M = M\{1-[e^{(-CvI/k)}]^n\}$$

Where:
M = fraction of infections resulting in morbidity
C = concentration of oocysts in water (oocysts/L)
v = fraction of oocysts that are infectious
I = volume of water ingested each day (L)
k = infectivity parameter
n = number of days of exposure
P_M = probability of disease

In the occurrence data, the Agency assumed that only a proportion of oocysts detected in the environment are infectious and that proportion was determined by use of data from microscopic examination of the oocysts. The proportion of *Cryptosporidium* oocysts in the environment that are infectious was estimated from the ICR and ICRSS data based on morphological appearance of oocysts and the proportion of oocysts with internal structures. These measures are more frequently used as a measure of viability than infectivity. Viability, usually evaluated by evidence of dye uptake, excystation or the presence of RNA, is a measure of the organism's ability to continue to survive as a living organism. Infectivity is usually defined as invasion and replication in a host cell, mouse model or human volunteers (analogous to infection). The set of organisms that are infectious is a subset of the set of organisms that are viable. Infectivity, not viability, is the relevant issue where the parameter is concerned.

The Agency analysis also used data on infectivity from a study by LeChevallier (2000). The data were expressed as a distribution with a range of 30 - 50%, mode = 40% (page 5-17). There is some evidence that polymerase chain reaction (PCR) detection of *Cryptosporidium* DNA in cell culture will give false positives because some oocysts may not be infectious but it is still possible to detect their DNA. Thus, direct detection of DNA by PCR may also pick up noninfectious oocysts that stick to the cell monolayer even if they have not infected the cells (Rochelle et al., 2001; De Leon and Rochelle, 2000). The Panel recommends that a careful

analysis of these issues be conducted and their impact on the risk reduction estimates be evaluated.

Infectivity of oocysts in the dose in the human challenge studies: The analysis of the human dose-response data assumes that 100% of the oocysts in the dose were infectious. However, it is likely that not all of the oocysts in the dose are "infectious". During its deliberations, the Panel discussed new data on cell culture infectivity and mouse infectivity that shows that approximately 5% of freshly excreted oocysts from a cow are "infectious" (see Upton et al.1994; Rochelle et al. 2001; Rochelle et al. 2002). It is important to clarify how the viability and/or infectivity of the oocysts used in the dose was evaluated. Was this based on excystation rate or on the morphological appearance of intact oocysts? It would also be helpful to verify the time between oocyst excretion and dosing volunteers (<2 weeks?) because this may affect the proportion of infectious oocysts in the various doses. The Panel recommends that EPA clarify these details on the conduct of the original study and include this clarification in its own documentation.

Use of human infectivity and cell infectivity data for the analysis: The Agency risk analysis incorporates viability determinations (a much weaker technique) and direct PCR-cell culture technique (which gives false positives). It is important that the Agency clearly indicate that human challenge data are currently limited to three strains necessitating the use of several major assumptions in the analysis. However, several strains have been studied in cell culture and in mouse infectivity assays. Since it is unclear whether these strains will ever be tested in human volunteers, it would be of value to compare the data between human, animal and cell culture lines. It would be useful for the Agency to consult with a number of researchers who have conducted infectivity studies on *Cryptosporidium* to gain a deeper understanding of how animal and cell infectivity ~~that~~ data might supplement the data on infectivity from human challenge studies. Further, it will be important to make broader use of statistical analysis as the Agency seeks to compare these differing types of infectivity data. The Panel recommends using the PCR-cell culture data as a supplement to the human infectivity data and clarify with the investigators the strengths, limitations and use of these data.

Proper statistical treatment of human challenge data from multiple isolates: As discussed above, there are some major concerns with the models for infectivity across strains. There are data from only three strains available to estimate the distribution of infectivity across strains. As a result, the distribution of infectivity derived from fitting the model relies heavily on both the assumed class of distributions (log normal) used and the assumed prior distribution for the standard deviation parameter F, which characterizes the variability of infectivity across strains. The Panel believes that the Agency could use a mixture of two distributions for infectivity to help characterize this uncertainty. The first component of the mixture will be a log normal distribution (with probability = 8) and the second component will be a log-t distribution with three degrees of freedom (with probability = 1 - lambda). The latter provides heavier tails and considers more extreme values for k to be more likely. Sensitivity analyses regarding the impact of the prior on sigma should also be performed.

The importance of genotype: It is correctly recognized that there are anthroponotic and zoonotic strains of *Cryptosporidium parvum*. One limitation of the infectivity data from human challenge studies is that currently only zoonotic strains (genotype 2) have been tested to date. However, most of the recognized *Cryptosporidium* outbreaks (foodborne and waterborne) have involved human genotypes. A human challenge study with a human genotype strain (genotype 1) is currently in progress and will provide valuable data for future risk assessments. The Panel recommends that when this data becomes available, the Agency reevaluate this risk assessment and the dose response model.

Variability in host susceptibility and the effect of previous infections: Variability in host susceptibility was not considered in the analyses of infectivity and morbidity. For example, the Agency dose-response model takes the number of oocysts as the dose surrogate. Thus the same approach is used to evaluate risk for infants and adults . The Panel recommends that the risk assessment consider explicitly the risk to susceptible populations (e.g., elderly, young, immunocompromised, etc.). These groups may be at greater risk of infection and/or disease due to greater water consumption per unit body weight, less effective immune systems, etc. Data from outbreak investigations may provide evidence of the consequences of infection for these populations.

Also, the analysis assumed that the exposed population had no previous immunity to *Cryptosporidium*. It is likely that the volunteers in the human challenge study are a mix of naive and previously exposed individuals, and that differences in host susceptibility and previous immunity had an effect on the estimates of the dose-response parameter. The Panel recommends that the agency compare its approach to this issue with the approach taken in other studies. Differences in host susceptibility and previous immunity will have an effect on the estimates of the infectivity parameter "k".

c) Morbidity Rate (pg 5-13)

The morbidity rate was defined as the probability of illness given infection and was estimated using a triangular distribution based on a range from Haas et al 1996. This rate may not be accurately estimated if asymptomatic infections were not detected in the human challenge studies. The greater the rate of asymptomatic infections, the more the probability of illness given infection will be underestimated.

In addition, the probability of illness given infection may be underestimated because these data are based on challenge studies in healthy adult volunteers. In the general population, there may be a greater probability of developing illness given infection because the whole population includes sensitive sub-populations that are more likely to develop symptomatic illness given infection.

Individuals with existing antibodies to *Cryptosporidium* may have a lower morbidity rate, although, data from Okhuysen et al., (1998) does not seem to support this. The Okhuysen, et al., experiment was conducted at relatively high doses, and there are no data on the morbidity rate at low doses in a population with previous *Cryptosporidium* infection. The high doses

employed may have overwhelmed any immune response in a way that low doses would not. If a significant fraction of the population carries antibodies, the incidence of disease might be significantly reduced.

The mortality rate in AIDS patients that was used in the economic analysis is based on old data from the 1993 Milwaukee outbreak. Current therapy has markedly reduced cryptosporidiosis mortality in AIDS cases. As a result, the mortality rate in this analysis is probably overestimated. At the same time, the mortality rate derived from Milwaukee may be too low for populations with a greater proportion of immunocompromised individuals.

The Panel recommends that these questions of morbidity rate, and their potential impact on the analysis of risk reduction, be more thoroughly analyzed and discussed in the document.

3.3.1.3 Exposure Assessment (pgs 5-14 - 5-24)

Exposure assessment in the Agency's analysis included estimation of: i) the distribution of total and infectious *Cryptosporidium* oocysts in finished water - derived from source water levels and estimated removal/inactivation from treatment; ii) the population served by systems potentially affected by the LT2ESWTR, and iii) the distribution of individual daily average drinking water consumption. The Panel has a number of comments on this assessment.

a) Estimates of Consumption (pg 5-22) require clarification.

There are a number of questions that arise in a review of the water consumption estimates used in the analysis. These questions should be more effectively addressed in the documentation. They include:

i) Why were two distributions of consumption used? What is the difference between them?
ii) Why are the median values (1.045, 0.71) lower than previous estimates of daily water consumption?
iii) Why was Distribution 1 used for the main analysis and Distribution 2 used in the analysis in the appendix?

Finally, it is not clear how the daily estimated consumption was extrapolated to annual exposure in Exhibit 5.8 (pg 5-23). Is individual consumption split between Community Water Systems and Non-Transient Non-Community Water Systems based on the estimated proportion of their time spent at home and at work or school or are individuals counted in both categories - i.e., total consumption counted twice. This estimate could be refined by age group. The Agency should examine water consumption patterns of the very young and very old because these are the most vulnerable age groups.

3.3.1.4 Results of the Risk Assessment

a) Estimates of Risk Require Clarification.

General approach to quantitative microbial risk assessment: Quantitative microbial risk assessment is a rapidly developing field. Previous work includes risk assessments by Haas et al., (1999)(see in NRC 2000), Perz, et al., (1998), and Teunis, et al., (1999) and an outbreak model done by Eisenberg, et al., (1998). The Panel recommends that a review of these and other preceding studies (including the sources of data, assumptions and statistical methods) be added to the document preamble. To the extent the approaches by these predecessors differ from the approach used by the Agency, the significance of the differences should be discussed and the reasoning behind the choices provided.

Discussions of uncertainty: The document should include a summary discussion of uncertainty and variability that is more detailed than that currently presented on pg 5-26. This discussion should include the following:

i) Identifying sources of uncertainty (already included on pg 5-26)
ii) Magnitude of uncertainty
iii) Effect of uncertainty on the estimate of risk
iv) Sensitivity analysis of which sources of uncertainty have the greatest impact on the estimate and the implications of this for future research efforts. It appears that uncertainty in estimates of risk and uncertainty in costs have different drivers. Uncertainty in estimates of risk was driven by dose-response data. Uncertainty in cost was driven by occurrence data (how the systems are classified into bins where action is necessary). Hence, it may turn out that uncertainty is much greater in cost than in estimates of risk or vice versa.
v) Identifying sources of variability (already included on pg 5-26). Sources of oocysts may be different for different communities (watersheds) animal sources vs human sources
    aa) Magnitude of variability
    bb) Effect of variability on the estimate of risk
    cc) Sensitivity analysis of what sources of variability have the greatest impact on the estimate

Significance of Assumptions: The document should also include a discussion of which assumptions may lead to an underestimate or overestimate of the risk and the benefits of the proposed regulation. For example, because the analysis only considered morbidity and mortality as outcomes, it is possible that the benefit is underestimated because the benefit of avoided infection was not considered. Avoiding infection in the community will reduce the potential for secondary transmission and additional cases and deaths. From a public health perspective, infection is the key outcome.

3.4 Charge 3: Treatment credits for four microbial toolbox options

EPA requested SAB comments on the treatment credits for four specific technologies included among its microbial toolbox options.

EPA provided the Panel with drafts of portions of the preamble to the LT2ESWTR, including: 1) a *Microbial toolbox overview* (US EPA 2001a), 2) *Off-stream raw water storage* (US EPA, 2001b), 3) *Pre-sedimentation* (US EPA 2001c), 4) *Lime softening* (US EPA, 2001d), and 5) *Lower finished water turbidity* (US EPA 2001e).

These draft documents were intended to provide the Panel with an understanding of the role and context of toolbox options in the LT2ESWTR and specific information on each of the four toolbox options that EPA asked the Panel to comment upon.

3.4.1 Panel Response to LT2ESWTR Charge Question 3

a) Comments on the Four Options

The Panel commends the EPA, as well as the stakeholder process used, for developing the bin classification framework for identifying the treatment requirements for drinking water and the microbial toolbox containing possible treatment options to guide systems having treatment needs. These alternatives add great flexibility for meeting varying water quality and treatment options and should result in safe drinking water for the people of the United States.

The Agency charged the Panel with evaluating EPA information on four of the toolbox options: 1) off stream raw water storage; 2) pre-sedimentation, 3) lime softening and 4) lower finished water turbidity. Specifically, the Agency asked the Panel to comment on the credits that have been proposed for specific toolbox options for *Cryptosporidium* removal.

In summary, the Panel recommends that no presumptive credits be given for off-stream storage and pre-sedimentation. It does agree with giving 0.5 log credit for two-stage lime softening if all the water is treated with both stages, and 0.5 log credit for plants that demonstrate a turbidity level in each individual filter effluent less than or equal to 0.15 NTU in at least 95 percent of the measurements taken each month. Details about these recommendations follow.

Off-Stream Storage: The data utilized by EPA in determining the appropriate credit for off-stream storage were derived from experiences in the United States as well as peer-reviewed literature from elsewhere in the world. The data show that there is variability in the removal of active oocysts in different reservoirs, due primarily to sedimentation, but also due to inactivation within the environment, both of which are governed to some degree by temperature and by residence time in the facility. After reviewing the supporting documentation, the Panel does not feel there are adequate data to demonstrate the proposed credits for off-stream storage and therefore recommends that no presumptive credits be given for this toolbox option. However, the Panel agrees that a particular utility should be able to take advantage of any removal achieved by this option by sampling after the off-stream storage facility for appropriate bin placement.

Pre-sedimentation: With regard to pre-sedimentation, many water treatment plants located on surface waters having large variations in water quality utilize pre-sedimentation as a treatment technique to remove large quantities of suspended material prior to input to an existing

conventional treatment plant or lime softening operation. The real purpose of pre-sedimentation is to provide for more consistent water quality prior to the conventional or lime softening treatment. In reviewing the literature provided by the Agency, not only on *Cryptosporidium*, but also on spore removal with both pilot as well as full-scale plants, it seems that the data are minimal in support of a 0.5 log presumptive credit for pre-sedimentation. As a result, the Panel feels that no credit should be given for pre-sedimentation. Additionally, the Panel feels performance criteria other than overflow rate need to be included if credit is to be given for pre-sedimentation. As with off-stream storage, the Panel does agree that a utility should be able to take advantage of this removal by sampling after the pre-sedimentation treatment process for appropriate bin placement.

Lime-softening: EPA proposes a 0.5 log credit toward *Cryptosporidium* treatment with lime softening plants that utilize two-stage softening. Based on the data provided, it appears that a 0.5 log of additional *Cryptosporidium* removal is an average number for a two-stage lime softening plant. Based on the data, single stage as well as two-stage lime softening generally outperforms conventional treatment due primarily to the heavy precipitation that occurs in lime softening reactors particularly when magnesium precipitation occurs. By treating water through a second precipitation reactor, additional removal should occur. However, depending on how the second reactor is utilized and the chemical feeds to the second reactor, the removal efficiencies vary significantly as presented in the literature. Therefore, the Panel supports an additional 0.5 log removal for two stage lime softening only if all the water passes through both stages. If a portion of the water bypasses the first stage, the Panel feels there should be no additional removal credit given.

Lower Finished-Water Turbidity: Finally, the additional credits for lower finished water turbidity seem to be consistent with what is known in both pilot and full-scale operational experiences for *Cryptosporidium* removal. As was contained in the Enhanced Surface Water Treatment Rule, lowering effluent turbidity in the treated water results in lower concentrations of *Cryptosporidium*. Therefore, it would be consistent to assume that even further lowering of turbidity would result in further reductions in *Cryptosporidium* in the effluent from filtration processes. It is also logical to assume that individual filter effluent turbidity meeting a specific criterion will provide for better water quality than for combined filter effluent meeting the same requirement. However, limited data were presented to show the exact removal that can be achieved using these two operational benchmarks. Based on the data provided, the Panel recommends that a 0.5 log credit be given to plants that demonstrate a turbidity level in each individual filter effluent less than or equal to 0.15 NTU in at least 95 percent of the measurements taken each month. No additional credit should be given to plants that demonstrate a combined filter effluent turbidity of 0.15 NTU or less.

b) Other Issues

The Panel's understanding of the approach used in developing the microbial toolbox is as follows. The additional log removals in the table of bin requirements are based in part on the assumption that conventional filtration plants in compliance with the Interim Enhanced Surface Water Treatment Rule (IESWTR) achieve an average of 3 logs removal of *Cryptosporidium*.

The Panel also understands that this assumption indicates that all conventional treatment plants can be expected to remove a minimum of 2 logs of *Cryptosporidium*. Furthermore, it is the Panel's understanding that an objective of the rule is to achieve an average oocyst concentration in treated surface waters of 10^{-4} oocysts/l or lower. Given the oocyst concentrations in bins 2, 3,and 4, and considering an average removal of 3 logs for conventional treatment, the additional removal requirements in bins 2, 3, and 4 are expected to provide an average treated water oocyst concentration of 10^{-4} oocyst/l or lower.

This approach differs from past regulatory approaches to *Giardia* and *Cryptosporidium* treatment credits and from present regulatory approaches to *Giardia* control. Current regulations for *Giardia* control provide 2.5 logs of removal credit when conventional treatment is used. It is the understanding of the Panel that this removal credit for *Giardia* is based on the minimum removal (not the average removal) achieved by these plants.

These differences between the IESWTR and LT2ESWTR regulations in the bases for assuming removal credits for *Giardia* and *Crypotosporidum* are not readily apparent and should be clarified and supported in the new regulations. Appropriate guidance will be needed for consistent implementation of these two regulations.

4. STAGE 2 DISINFECTION BYPRODUCTS RULE

4.1 Charge 1: Initial Distribution System Evaluation (IDSE):

EPA requests SAB comment on whether the IDSE is capable of identifying new compliance monitoring points that target high TTHM and HAA5 levels and whether it is the most appropriate tool available to achieve this objective.

EPA provided the Panel with two draft documents on the Initial Distribution System Evaluation that is to be proposed in the S2DBP rule. Information provided in support of Charge question 2 below in this section also bears some relevance to this question. The documents provided by EPA include:

a) *"E. Initial distribution system evaluation (IDSE)"* (US EPA, 2001f) a draft overview of the IDSE intended for the preamble of the rule; and

b) Stage 2 Disinfectants and Disinfection Byproducts Rule Initial Distribution System Evaluation Guidance Manual (The Cadmus Group, Inc., 2001d) which provides recommendations for how utilities should proceed to determine monitoring sites to reflect the highest levels of TTHM and HAA5 occurrence within the distribution system.

4.1.1 Panel Response to S2DBP rule Charge Question 1.

4.1.1.1 IDSE Effectiveness

The Panel believes that the proposed Initial Distribution System Evaluation (IDSE) is capable of identifying new compliance monitoring points that target higher DBP levels than are currently monitored in the existing compliance monitoring programs for the THM Rule and Stage 1 DBP Rule. However, the IDSE may not identify the highest levels to which consumers in a given distribution system are exposed. The basis for the latter statement is that the IDSE does not consider short-term, temporal variations that occur at different sites in the distribution system due to varying (e.g. diurnal) water demands and distribution system architecture and operation. Distribution systems are, by their nature, highly dynamic. Varying water demand patterns (e.g. low density and high density residential water use, industrial and commercial water use, irrigation) and operating conditions (e.g. pumping patterns and storage tank operations) normally lead to appreciable temporal and spatial variations in hydraulic residence times (water age) and water quality throughout the system that are not captured by the proposed IDSE. Hence, it is unlikely that a single grab sample taken at any site at any time will yield a representative DBP concentration for that site, and that grab samples taken at a number of sites will identify sampling sites with the highest DBP concentrations.

Further, rates of disinfection byproduct formation and degradation are temperature-dependent and may change on a seasonal basis. Coupling this with the fact that water demand patterns, and therefore hydraulic residence times, also may change with season may mean that

peak DBP levels migrate from the remote parts of the system during colder months to interior portions of the system during warmer months. Furthermore, this behavior will probably not be consistent from one DBP to the next.

Therefore, the Panel believes that it is important that site selection be re-evaluated periodically. In rapidly growing utilities changes in the distribution system architecture and flow patterns are common. As a result, the sites with high DBP levels often change. Significant changes also occur in systems that are not rapidly growing as components fail and/or improvements are made. If sample locations are not updated with time to reflect these changes in distribution system behavior, then the sample locations may lose their relevance over time. Further, the IDSE is only a 12-month program, and utilities and primacy agencies have no assurances that the 12-month period over which the IDSE is performed will indeed be typical of normal system operations. The Panel recommends that temporal limitations be identified in the documentation and that periodic re-evaluation of selected sites be required so that changes in the system and/or its use will be addressed.

4.1.1.2 IDSE Appropriateness

The EPA also asked if the IDSE is the most appropriate tool to reach the objective of identifying new compliance monitoring points that target higher THM4 and HAA5 levels. The Panel believes that the proposed standard monitoring program (SMP) for sub-part H systems serving more than 10,000 people, in which 8 samples are collected at 2-month intervals, is reasonable. The Panel does recommend, however, that the 8 samples be re-allocated so that, for both free chlorine and chloramines, 3 samples be taken at potential high THM4 sites, 3 samples be taken at potential high HAA5 sites, and only 1 sample each be taken at an average site and at the point of entry to the system. If indeed the objective is to locate and monitor the sites with high THM4 and high HAA5 concentrations, more samples need to be allocated to this objective. One point of entry site is sufficient to gauge the initial concentration of DBPs entering the system, and only one "average" site should be sufficient to maintain connectivity to the existing compliance monitoring program. The Panel also believes that the "average" site for the IDSE should be one of the average locations in the existing Stage 1 DBP compliance monitoring program. This would mean that every 6 months (twice during the IDSE), utilities would only have to take 7 samples as part of the IDSE, with the eighth sample being one of the compliance monitoring samples.

The Panel also recommends that the IDSE should require the measurement and reporting of residual chlorine (free or combined) concentrations at the time of DBP sample collection, and that individual THM and HAA species be reported in addition to the aggregate concentrations. The Panel also suggests that the IDSE recommend that complimentary pH, temperature, and heterotrophic plate count be measured and recorded concurrently with DBP measurements. Such information will prove to be valuable to the utilities, the primacy agencies, and the EPA in the future.

With respect to time of sample collection, there is no reason to believe that THM4 or HAA5 levels will be highest in the morning. In view of the dynamic and highly complex nature

of water distribution systems, it is equally likely that THM4 or HAA5 levels at some locations will be highest in the evening. The Committee recommends that the reference to time of sample collection be omitted from the Guidance Manual (e.g. p. 2.9 of Guidance Manual) and be left to the discretion of the utilities and their respective primacy agency.

The Panel also recommends that EPA provide more guidance to the utilities with respect to identifying potential sampling sites with the highest HAA5 concentrations. The only reference in which some guidance is provided is on page 5-18, line 39 of the Guidance Manual, although that guidance is not especially clear. It might be expected that, at least in waters with temperatures supporting microbial activity, HAA5 levels may decrease when free chlorine residuals decrease below 0.2-0.3 mg/l or combined chlorine residuals decrease below 0.5 mg/l. This may not be the case in cold waters in which microbial activity is minimal; in such cases, high HAA5 sites may coincide with high THM4 sites. Distribution system dynamics, water age, chlorine residual data, and heterotrophic plate count data should be examined in selecting sample sites.

The Panel also recommends that EPA require that the selection of monitoring sites be justified rather than simply recommending that they be justified (p. 1-4, line 14), and that the IDSE report provide justification for the selection of sites (p. 5-24, line 16) (The Cadmus Group, Inc., 2001d).

The Panel believes that the proposed system specific studies (SSS) approach described in Chapter 6 of the Guidance Manual needs improvement if sound guidance is to be provided to the utilities. Water consumption (demands) should be more accurately simulated in the network model, given the availability of such information. It is important to realize that different types of water users will consume water at different times and rates during the day. Water demands should be classified and allocated based on their water use type (domestic, industrial, commercial, etc.) and each type of water user should be assigned an individual water use pattern over a 24-hour (or other) period. Estimates of demand distributions could be obtained by using land use information or by using a water meter or assessor's parcel number location methodology (geocoded meter location). For example, the land use computation method consists of intersecting demand area polygons with land use polygons using water duty factors to create water demands for selected analysis nodes. The geocoded meter location method consists of grouping water billing data into demand areas around analysis nodes by using a spatial reference of water meters, yielding a credible demand distribution as demands are allocated per customer billing accounts (and automatically taking into account vacant parcels and large water users). Other spatial demand allocation methods include assigning geocoded customer meters to the nearest analysis node or to the nearest pipe and then split the demand among the bounding analysis nodes. Some care will be required to ensure that demands are accurately allocated according to actual spatial consumption.

4.1.1.3 Other Considerations

The Panel has a number of concerns that it considers to be of significance but which do not easily fit into the other two charge questions on the S2DBP Rule. These are discussed in the following paragraphs.

Clarification of Assumptions: A number of assumptions and policy decisions were made in the development of the form of the Stage 2 DBP Rule and the IDSE. These need to be stated at the outset and made clear throughout the documentation in support of the rule. These include:

i) the decision to continue to regulate THM4s and HAA5s collectively as group parameters rather than as individual species;
ii) the decision to continue to regulate only five of the HAAs (HAA5) rather than all nine bromine- and chlorine-containing HAAs (HAA9);
iii) recognition of the fact that, for purposes of simplicity, the IDSE overlooks short-term temporal variability in the selection of sites for locating and monitoring maximum levels of THM4s and HAA5s;
iv) recognition of the fact that sampling and monitoring costs were key considerations in designing the requirements for the standard monitoring program for the IDSE;
v) recognition of the fact that, although the Source Water Analytical Tool (SWAT) model was developed for modeling the effects of treatment on DBP formation and was not developed to model changes in individual or aggregate DBP concentrations in distribution systems, it was the only tool that the EPA had for purposes of the benefits analysis in support of the Stage 2 Rule.

Use of the SWAT Model: In the risk reduction analysis, the SWAT model is used to predict monthly DBP concentrations both under current conditions and under conditions where plant modifications have been made to meet the requirements of Stages 1 and 2 (sections 3.7.2 and 5.4.1.1)(The Cadmus Group, Inc., 2001e). This use of the SWAT model would be appropriate if it could be relied upon for valid predictions in such applications. Unfortunately, EPA has not demonstrated that this is the case. Large discrepancies exist between SWAT predictions and ICR data, and these discrepancies raise serious questions regarding both the accuracy of the SWAT model and the adequacy of attempts to characterize DBP concentrations of dynamic systems with such a limited number of samples (four sites with four samples per year).

Two aspects of data presentation in the Stage 2 DBPR Economic Analysis serve to illustrate how the discrepancies are under-represented -- (1) the use of cumulative frequency distributions (pages 3-31 and A-18 through A20)(The Cadmus Group, Inc., 2001e), and (2) miscalculation of "mean predicted errors" (page A-34 and Exhibit A.21). The problem with the use of cumulative frequency diagrams is that such plots have the same shape even when paired values have little agreement. Plants with low THM4 or HAA5 from the SWAT model are not necessarily the same plants with low THM4 or HAA5 plants from the ICR data. This discrepancy is totally lost when the data are presented as cumulative frequency curves. In the calculation of the "mean predicted error," "the absolute value of the difference between "SWAT

annual plant mean" and "ICR annual plant mean" should have been used instead of signed values, or an R^2 value should have been calculated. The way the calculation was done, positive deviations canceled out negative deviations thereby grossly underestimating "mean predicted errors." The graphical results of pages A-23 to A33 convey a much greater sense of the discrepancies between the SWAT predictions and the ICR data. The magnitude of these discrepancies diminishes the value of the subsequent use of either SWAT or ICR data in Economic Analyses or risk reduction calculations.

The limitations to the model's accuracy arise from the inherent limitations of the existing state of the art for predicting DBP concentrations from water quality data and/or the inherent limitations in the available database, and hence cannot be easily fixed. Under the circumstances, the contribution that the model can make to an evaluation of the risk reduction from the Stage 2 rule is marginal at best. The Panel recommends that either this portion of the analysis of the risk reduction be eliminated or that the presentation be altered to reflect the uncertainties associated with use of the model.

Monitoring Frequency Under the IDSE: Though this is a relatively minor point, it should be made clear, in all documents relevant to the Stage 2 Rule, that quarterly monitoring of DBPs means every 3 months. For example, Table 5.4 and page 192 (US EPA, 2001h) do not unequivocally indicate that the basis for the LRAA calculation is sampling at 3-month intervals rather than once each quarter as in the current THM Rule and Stage 1 Rule.

4.2 Charge 2: Public Health Protection of S2DBPR:

4.2.1 Panel Response to S2DBPR Charge Question 2.

EPA requests SAB comment on whether the locational running annual average (LRAA) standards for total trihalomethanes (TTHMs) and haloacetic acids (HAA5), in conjunction with the Initial Distribution System Evaluation of the proposed S2DBP rule, more effectively achieves public health protection than the current running annual average (RAA) standards, given the existing knowledge of DBP occurrence and the available health effects data.

EPA is concerned with reproductive, developmental, and carcinogenic effects which are associated with TTHMs and HAAs. EPA intends to reduce the variability of exposure to DBPs for people at different points in the distribution system, and therefore reduce risks.

EPA provided the Panel with documents that gives the Agency's case for why it believes there is a health concern for disinfection byproducts. Documents provided to the Panel in support of the Health concerns determination include:

a) a draft of preamble section *"III. Public Health Risk"* (US EPA, 2001g) that briefly discusses reproductive and developmental epidemiology information received after the Stage 1 DBP rule;

b) Quantification of Bladder Cancer Risk from Exposure to Chlorinated Surface Water (US EPA, 1998) which provides details on the population attributable risk concept used to quantify the estimated number of cancer cases that would be attributable to the consumption of chlorinated drinking water;

c) Reproductive and Developmental Effects of Disinfection By-Products (Reif et al., 2000) which provides a critical review of the epidemiologic literature pertaining to reproductive and developmental effects of exposure to disinfection byproducts in drinking water;

d) Review of Animal Studies for Reproductive and Developmental Toxicity Assessment of Drinking Water Contaminants: Disinfection By-Products (DBPs) (Tyl, 2000), which provides a review of the animal reproductive and developmental toxicity data on disinfection byproducts; and

e) *"V. Discussion of Proposed Stage 2 DBPR Requirements"* (US EPA, 2001h) which explains how the chloroform MCLG was developed.

One document was provided to support evaluation of charge question 2 in the area of "Occurrence/Reduction of Peaks":

a) *Excerpts from the Economic Analysis for the Stage 2 Disinfectants and Disinfection Byproducts Rule* (The Cadmus Group, Inc., 2001e) which indicates the extent to which EPA estimates that DBP peaks might be reduced by the proposed S2DBPR.

One document was provided to support evaluation of charge question 2 in the area of "Monitoring Requirements and Compliance Determination":

a) *G. Monitoring requirements and compliance determination*. (US EPA, 2001i).]

EPA issued a Stage 1 DBP regulation that requires regulated water systems to meet a standard of 80 ug/l Total Trihalomethanes (THM4) and 60 ug/l for five Haloacetic Acids (HAA5) as well as other DBPs during 1998. Consistent with the original THM rule, the regulation requires that systems implement a Running Annual Average (RAA) approach to monitoring for these contaminants and that they be kept at or below these levels. In arriving at these standards, EPA recognized, as does this Panel, that the regulated THM4 and HAA5 which are prominently identified in the rule, are not the only DBPs in these classes which could be in drinking water, nor are these classes the only possible DBPs in chlorinated or other drinking water systems. However, the Agency and a large group of stakeholders who were involved in an extensive series of negotiations, agreed that it was appropriate to focus on these DBPs in the policy embodied in the Stage I standard. They further agreed that it was reasonable to assume that the controls that would be implemented for reducing levels, and therefore risks, of those regulated DBPs, would also reduce risks from other DBPs that are, as yet, to be identified and/or studied for health effects.

The panel is generally supportive of the THM4 and HAA5 actions under consideration. Although the epidemiology data associating cancer with chlorinated drinking water has resulted in relatively small odds ratios, the observations have now been consistent across a broad number of studies with varying degrees of increasing sophistication, especially for bladder cancer. While the odds ratios are small, the numbers of attributable cases are large relative to other environmental issues of concern (Morris et al., 1992; Poole, 1997). Therefore, the epidemiology data can be taken to indicate that there is a problem that needs to be taken seriously. The THM4 and HAA5 standards reviewed by the Panel are a constructive interim step towards addressing this problem.

The Panel also agrees that establishing an LRAA would be expected to reduce exposure to the nine compounds that are regulated. As detailed in section 4.1.1.1 of this document, which discusses the dynamics of water movement through the distribution system and on-going production and degradation of disinfection by-products, it is uncertain that the requirements of the IDSE will result in a sufficiently complete distribution system characterization to be confident that the locations with the highest exposure will be identified and therefore that all the households will gain the protection of the new standards. Nevertheless, the variability in exposure to regulated DBPs, from one point in the system to another, will be reduced, particularly at the extreme locations that the IDSE does identify, and the consumers at those locations will have lower levels of exposure to the measured DBPs.

There is also a policy issue associated with the regulatory approach that the panel suggests the EPA give greater visibility. The RAA does not identify locations with consistently higher concentrations of DBPs and the LRAA is designed to do so. Despite the difficulties associated with developing precise estimates of benefits resulting from a switch from the RAA to the LRAA, the LRAA provides greater equity among consumers, i.e., with the LRAA, a larger segment of U.S. consumers will drink water at or below the MCL. The committee suggests that this issue be given greater prominence in arguments supporting the LRAA.

Assessments of health risk reduction from this rule have emphasized reductions in bladder cancer risk. It is important to address bladder cancer because epidemiological data suggest that lifetime consumption of chlorinated surface water poses a bladder cancer risk approaching one in one thousand (Morris et al., 1992; Poole, 1997). There are other serious putative health effects that have been identified from toxicological studies of individual disinfection byproducts. These include risks of other cancers, impairment of male and female reproduction, and effects on developing organisms. Collectively, the risks calculated from these toxicological studies are 1-2 orders of magnitude less than the bladder cancer risks suggested by the epidemiology studies. The bladder cancer may well be due to agents other than the THM4 and HAA5 species (Bull et al., 2001) While based on more limited evidence, reductions in reproductive health risks are considered to be a benefit of the rule; however the lack of data preclude quantification of this benefit.

On the other hand, the panel cautions that EPA has not satisfactorily demonstrated that promulgating the S2DBP rule will result in the reduction in bladder cancer risk which has been projected. The following are the reasons for this statement:

1. The disinfectant by-product mixture produced when water is chlorinated is extremely complex, and within a given system, varies considerably.
2. The specific by-products resulting in increased bladder cancer have not been identified, but are unlikely to be accounted for by the aggregate THM4 or HAA5[4] concentrations.
3. It has not been demonstrated that actions taken to control the collective THM4 and HAA5 concentrations will also control other known and unknown by-products.
4. Treatment technologies may emerge that target only the regulated by-products, without addressing the rest of the DBP mixture.
5. Some technologies aimed at reducing the target DBPs might result in new DBPs of unknown signficance[5].

In summary, it is the Panel's opinion that cancer and reproductive health risks likely result from water chlorination, and that reasonably good estimates of such risks can be derived from epidemiological data However, EPA has not demonstrated that the health risk reductions that accrue from the proposed rule will be proportional to the reductions in the THM4 and HAA5 concentrations. Some health benefits in addition to those specifically attributable to these classes of DBPs could accrue, but only to the extent that the measures that water systems take to reduce these byproducts also reduce the concentrations of other byproducts. It should be remembered that changing treatment has some potential to change the by-product mixture produced and some of the new compounds generated could be more harmful. Nevertheless, the Panel believes that some risk reduction will occur and that speculation such as that discussed above should not delay the promulgation of the present rule.

[4] For example, the target DBPs being regulated may not be good surrogates for the compounds that produce the reproductive toxicities. The risks identified in the epidemiology studies are much greater than those suggested by the studies of these individual by-products in animals. It is important to note, that the target DBPs do not include the most potent reproductive toxicant among the DBPs examined to date, bromochloroacetic acid.

[5] The recent identification of N-nitroso-N-dimethylamine (NDMA) as a by-product of chloramination is an example. NDMA belongs to a class of chemical carcinogens which contains some members that are known to produce bladder cancer in rats. NDMA is between 3 and 4 orders of magnitude more potent as a carcinogen than the THM4 and HAA5 (U.S. EPA,1997). Perhaps the most common method used for controlling THM4 and HAA5 formation is to use chlorine combined with ammonia for residual control. Recent work has shown that this combined chlorine can result in increased NDMA formation (Najm and Trussell, 2002, Choi and Valentine, 2002, Mitch and Sedlak, 2002).

REFERENCES

Bull, R.J., Krasner, S.W., Daniel, P.A., and Bull, R.D. 2001. Health Effects and Occurrence of Disinfection By-Products. Awwa Research Foundation and American Water Works Foundation, Denver, CO, pp. 1-13.

Choi, J. H.; Valentine, R. L., 2002, "Formation of *N*-nitrosodimethylamine (NDMA) by reaction of monochloramine in a model water: a new disinfection by-product." *Wat. Res.V36*, pp817-824.

De Leon, R. and P. Rochelle. (2000) Quantitative Cell Culture-based Infectivity Assay for *Cryptosporidium parvum* in Water. Report of a STAR grant. Metropolitan Water District of Southern California. Water Quality Laboratory, La Verne, CA; R-825146.

Eisenberg JN, Seto EY, Colford JM Jr, Olivieri A, Spear RC. (1998). An analysis of the Milwaukee cryptosporidiosis outbreak based on a dynamic model of the infection process. Epidemiology. 9(3):228-31]

Haas, C.N., C. Crockett, J.B. Rose, C. Herba, A.Fazil. (1996). Infectivity of *Cryptosporidium parvum* oocysts. Journal WWA 88(9): 131-136.

Haas, et al. (1999). NRC (2000) Committee to Review the New York City Watershed Management Strategy. (2000) *Watershed Management for Potable Water Supply: Assessing New York City Approach.* Water Science and Technology Board, National Research Council, National Academy Press, Washington, DC.

LeChevallier, M.W., J.L. Clancy, Z. Bukhari, S. Bukhari, T. Hargy, J.S. Rosen, J. Sobrinho, M.M. Frey. (2000) Source Water Assessment: Variability of Pathogen Concentrations (paper presented at the 2000 WQTC).

MacKenzie WR, Schell WL, Blair KA, Addiss DG, Peterson DE, Hoxie NJ, Kazmierczak JJ, Davis JP. Massive outbreak of waterborne cryptosporidium infection in Milwaukee, Wisconsin: recurrence of illness and risk of secondary transmission. Clin Infect Dis 21(1):57-62

Mitch, W. A.; Sedlak, D. L., 2002, "Formation of N-nitrosodimethylamine (NDMA) from dimethylamine during chlorination." *Environ. Sci. Technol.V36,* pp588 -595.

Millard P, K Gensheimer, DG Addiss, DM Sosin, GA Beckett, A HouckJankoski, A Hudson (1994). An outbreak of cryptosporidiosis from fresh pressed apple cider JAMA 272(20):1592-1596]

Najm, I.; Trussell, R. R., 2001, "NDMA Formation in Water and Wastewater." *Journal AWWA, V93,* pp 92-99, 2001, February, 92-99.

National Research Council (NRC, 2000). Watershed Management for Potable Water Supply: Assessing the New York City Strategy. Chapter 6. Tools for Monitoring and Evaluation. Committee to Review the New York City Watershed Management Strategy, Commission on Geosciences, Environment and Resources. National Academy Press, Washington DC.

Newman RD, Zu SX, Wuhib T, Lima AA, Guerrant RL, Sears CL (1994). Household epidemiology of Cryptosporidium parvum infection in an urban community in northeast Brazil. Ann Intern Med 120(6):500-5

Okhuysen, PC, CL Chappell, CR Sterling, W Jakubowski and HL DuPont. (1998) Susceptibility and serologic response of healthy adults to reinfection with *Cryptosporidium parvum. Infection and Immunity.* 66(2):441-443.

Perz, JF, JK Ennever and SM LeBlancq. (1998) *Cryptosporidium* in tap water: Comparison of predicted risks with observed levels of disease. American Journal of Epidemiology. 147(3):289-301.

Puech MC, McAnulty JM, Lesjak M, Shaw N, Heron L, Watson JM. (2001) A statewide outbreak of cryptosporidiosis in New South Wales associated with swimming at public pools. Epidemiol Infect 126(3):389-9]

Reif, JS, Bachand, A, and Andersen, M (2000). *Reproductive and Developmental Effects of Disinfection By-Products*. Prepared for Health Canada. Colorado State University, Dept. of Environmental Health, Fort Collins, CO, October 31, 2000.

Rochelle, PA, DM Ferguson, DM Johnson, and R. DeLeon. (2001). Quantitation of *Cryptosporidium parvum* infection in cell culture using a colorimetric *in situ* hybridization assay. *J. Eukaryot. Microbiol.* 48:565-574.

Rochelle, PA, MM Marshall, JR Mead, AM Johnson, DG Korich, JS Rosen and R. DeLeon. (2002). Measurement of *Cryptosporidium parvum* infectivity: *in vitro* cell culture compared to a mouse assay. *Applied and Environmental Microbiol.* submitted.

Sorvillo, FJ, MPH, K Fujioka, PhD, M Tormey, MPH, R Kebabjian, RS, W Tokushige, L Mascola, MD, S Schweid, M Hillario, SH Waterman, MD (2001). Epidemiologic Notes and Reports Swimming-Associated Cryptosporidiosis -- Los Angeles County. MMWR 39(20);343-345

Teunis, PFM and AH Havelaar. (1999) *Cryptosporidium* in drinking water: Evaluation of the ILSI/RSI quantitative risk assessment framework. Rijksinstituut voor Volksgezondheid en Lilieu, RIVM report number 284550006.

The Cadmus Group, Inc. (2001a). *Occurrence and Exposure Assessment for the Long Term 2 Enhanced Surface Water Treatment Rule.* Report under Contract 68-C-00-113, August 27, 2001, Fifth Draft.

The Cadmus Group, Inc. (2001b). *Economic Analysis for the Long Term 2 Enhanced Surface Water Treatment Rule* 9. Report under Contract 68-C-00-113, August 27, 2001, Fifth Draft.

The Cadmus Group, Inc. (2001c). *Appendices to the Economic Analysis for the Long Term 2 Enhanced Surface Water Treatment Rule.* Report under Contract 68-C-00-113, August 27, 2001, Fifth Draft.

The Cadmus Group, Inc. (2001d). *Stage 2 Disinfectants and Disinfection Byproducts Rule Initial Distribution System Evaluation Guidance Manual.* Report under Contract 68-C-99-206, August 22, 2001, Fourth Draft.

The Cadmus Group, Inc. (2001e) *Excerpts from the Economic Analysis for the Stage 2 Disinfectants and Disinfection Byproducts Rule.* Report under Contract 68-C-99-206, August 24, 2001, Seventh Draft revised.

Tyl, RW (2000). *Review of Animal Studies for Reproductive and Developmental Toxicity Assessment of Drinking Water Contaminants: Disinfection By-Products (DBPs)*. Research Triangle Institute. October 12, 2000.

Upton, SJ, M Tilley and DB Brillhart (1994). Comparative development oc *Cryptosporidium parvum* in 11 continuous cell lines. *FEMS Microbiol. Letters.* 118:233-236.

USEPA (1997). Integrated Risk Information System. N–Nitrosodimethylamine; CASRN 62-75-9.

US EPA (1998). *Quantification of Bladder Cancer Risk from Exposure to Chlorinated Surface Water.* US EPA, Office of Water, Office of Science and Technology. August 26, 1998.

US EPA (2000) *Stage 2 Microbial and Disinfection Byproducts Federal Advisory Committee Agreement in Principle.* FR 65, No. 251:pp83015-83024, December 29, 2000.

US EPA. (2001a). *Microbial toolbox overview.* Draft document prepared by the US EPA Office of Ground Water and Drinking Water and transmitted to the SAB via an email from Dr. D. Schmelling, September 4, 2001.

US EPA. (2001b). *Off-stream raw water storage.* Draft document prepared by the US EPA Office of Ground Water and Drinking Water and transmitted to the SAB via an email from Dr. D. Schmelling, September 4, 2001.

US EPA (2001c). *Pre-sedimentation*. Draft document prepared by the US EPA Office of Ground Water and Drinking Water and transmitted to the SAB via an email from Dr. D. Schmelling, September 4, 2001.

US EPA (2001d). *Lime softening*. Draft document prepared by the US EPA Office of Ground Water and Drinking Water and transmitted to the SAB via an email from Dr. D. Schmelling, September 4, 2001.

US EPA (2001e). *Lower finished water turbidity*. Draft document prepared by the US EPA Office of Ground Water and Drinking Water and transmitted to the SAB via an email from Dr. D. Schmelling, September 4, 2001.

US EPA (2001f). Draft of preamble section . Initial distribution system evaluation (IDSE) Undated.

US EPA (2001g). Draft of preamble section *II. Public Health Risk* Undated. Pages 77-116.
US EPA (2001h). Draft of preamble section . *Discussion of Proposed Stage 2 DBPR Requirements. Undated. Pages 155-202.*

US EPA (2001i). Draft of preamble section . *Monitoring requirements and compliance determination. Undated.*

ATTACHMENT A

ACRONYMS AND ABBREVIATIONS

BAT	Best Available Treatment
cdf	Cumulative Distribution Frequency
CWS	Community Water System
DBP	Disinfection Byproducts
DWC	Drinking Water Committee
EPA	U.S. Environmental Protection Agency
HAA5	Haloacetic Acids
HAN	Haloacetonitriles
ICR	Information Collection Rule
ICRSS	Information Collection Rule Supplemental Survey
IDSE	Initial Distribution System Evaluation
IESWTR	Interim Enhanced Surface Water Treatment Rule
LRAA	Locational Running Annual Average
LS	Lime Softening
LT2ESWTR	Long Term 2 Enhanced Surface Water Treatment Rule
MCL	Maximum Contaminant Level
MCLG	Maximum Contaminant Level Goal
NTNCWS	Non-transient Non-community Water Systems
PCR	Polymerase Chain Reaction
POTW	Publically Owned Treatment Works
RAA	Running Annual Average
SAB	U.S. EPA Science Advisory Board
SDWA	Safe Drinking Water Act Amendments of 1996
SWAT	Surface Water Analytical Tool
S2DBPR	Stage 2 Disinfection/Disinfectant Byproduct Rule
THM	Trihalomethanes
TTHM	Total Trihalomethanes